

In the Claims:

1. (Currently Amended) A procytotoxin comprising a **cytotoxic** peptide having at least one lysine residue bound via a peptide bond to at least one amino acid via the ϵ -amino group of said lysine residue, wherein said peptide without said modification is a cytotoxic peptide, and wherein said at least one amino acid bound via the ϵ -amino group of said lysine residue acts to prevent the peptide from forming a lytically active conformation.

2. (Previously Amended) The procytotoxin of claim 1, wherein the cytotoxic peptide is a pore-forming cytolytic peptide.

3. (Currently Amended) The procytotoxin of claim 2, wherein the pore-forming cytolytic peptide is selected from the group consisting of Ae I, cytolysin of sea anemone, aerolysin, amatoxin, amoebapore, amoebapore homolog from *Entamoeba dispar*, brevinin-1E, brevinin-2E, barbatolysin, cytolysin of *Enterococcus faecalis*, delta hemolysin; diphtheria toxin, El Tor cytolysin of *Vibrio cholerae*, equinatoxin, enterotoxin of *Aeromonas hydrophila*, esculentin, granulysin, haemolysin of *Vibrio parahaemolyticus*, intermedilysin of *Streptococcus intermedius*, the lentivirus lytic peptide, leukotoxin of *Actinobacillus actinomycetemcomitans*, magainin, melittin, membrane-associated lymphotoxin, Met-enkephalin, neokytorphin, neokytorphin fragment 1, neokytorphin fragment 2, neokytorphin fragment 3, neokytorphin fragment 4, NK-lysin, paradaxin, perforin, perfringolysin O, theta-toxin, of *Clostridium perfringens*, phallolysin, phallotoxin, streptolysin, **and** analogs thereof, and derivatives thereof.

4. (Original) The procytotoxin of claim 3, wherein the cytolytic peptide is selected from the group consisting of amoebapores, amoebapore analogs and amoebapore derivatives.

5. (Previously Amended) The procytotoxin of claim 4, having the following structure: Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys(R)-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys(R)-Leu-Ile-Gln-Leu-Ile-Glu-Asp-Lys(R), wherein at least one (R) is independently selected from the group consisting of $[\epsilon-\gamma]$ -Glu, $[\epsilon-\gamma]$ -Glu- $[\alpha-\gamma]$ -(Glu)₁₋₃, $[\epsilon-\alpha]$ -(Phe)₁₋₃, $[\epsilon-\alpha]$ -(Tyr)₁₋₃, $[\epsilon-\alpha]$ -(Trp)₁₋₃, $[\epsilon-\alpha]$ -(Lys)₁₋₃ and $[\epsilon-\alpha]$ -(Arg)₁₋₃, wherein $[\epsilon-\gamma]$ represents a peptide bond between

the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate, $[\alpha-\gamma]$ represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate, $[\epsilon-\alpha]$ represents a peptide bond between the epsilon amino acid of lysine and the alpha carboxyl group of the indicated amino acid and the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

6. (Original) The procytotoxin of claim 3, wherein the cytolytic peptide is a melittin, a melittin analog or a melittin derivative.

7. (Original) The procytotoxin of claim 6, having the following structure: Gly-Ile-Gly-Ala-Val-Leu-Lys(R)-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Lys(R)-Arg-Lys(R)-Arg-Gln-Gln, wherein R is independently selected from the group consisting of the unmodified ϵ -amino group of the adjacent lysine residue, $[\epsilon-\gamma]$ -Glu, $[\epsilon-\gamma]$ -Glu- $[\alpha-\gamma]$ -(Glu)₁₋₃, $[\epsilon-\alpha]$ -(Phe)₁₋₃, $[\epsilon-\alpha]$ -(Tyr)₁₋₃, $[\epsilon-\alpha]$ -(Trp)₁₋₃, $[\epsilon-\alpha]$ -(Lys)₁₋₃ and $[\epsilon-\alpha]$ -(Arg)₁₋₃, wherein $[\epsilon-\gamma]$ represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate, $[\alpha-\gamma]$ represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate, $\epsilon-\alpha]$ represents a peptide bond between the epsilon amino group of lysine and the alpha carboxyl group of the indicated amino acid and the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

8. (Original) The procytotoxin of claim 1 having a structure selected from the group consisting of: N-Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys-Ile-Gln-Leu-Ile-Glu-Asp-Lys($[\epsilon-\gamma]$ -Glu- $[\alpha-\gamma]$ -Glu)-COOH and NH₂-Gly-Ile-Gly-Ala-Val-Leu-Lys-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Lys($[\epsilon-\gamma]$ -Glu- $[\alpha-\gamma]$ -Glu)-Arg-Lys($[\epsilon-\gamma]$ -Glu- $[\alpha-\gamma]$ -Glu)-Arg-Gln-Gln-COOH.

9. (Original) A pharmaceutical composition, comprising the procytotoxin of claim 1, and a pharmaceutically acceptable excipient.

10. (Original) A method for selectively destroying a target cell, comprising contacting the target cell with a procytotoxin, which comprises a cytotoxic peptide having at least one lysine residue bound via a peptide bond to at least one amino acid via the ϵ -amino group of said lysine residue.

11. (Original) The method of claim 10, wherein the cell is a cancer cell.

12. (Original) The method of claim 11, wherein said cancer cell is selected from the group consisting of prostate, ovarian, lung and skin cells.

13. (Original) The method of claim 11, wherein the cytotoxic peptide is a pore-forming cytolytic peptide.

14. (Original) The method of claim 13, wherein the pore-forming cytolytic peptide is selected from the group consisting of Ae I, cytolysin of sea anemone, aerolysin, amatoxin, amoebapore, amoebapore homolog from *Entamoeba dispar*, brevinin-1E, brevinin-2E, barbatolysin, cytolysin of *Enterococcus faecalis*, delta hemolysin, diphtheria toxin, El Tor cytolysin of *Vibrio cholerae*, equinatoxin, enterotoxin of *Aeromonas hydrophila*, esculentin, granulysin, haemolysin of *Vibrio parahaemolyticus*, intermedilysin of *Streptococcus intermedius*, the lentivirus lytic peptide, leukotoxin of *Actinobacillus actinomycetemcomitans*, magainin, melittin, membrane-associated lymphotoxin, Met-enkephalin, neokytorphin, neokytorphin fragment 1, neokytorphin fragment 2, neokytorphin fragment 3, neokytorphin fragment 4, NK-lysin, paradaxin, perforin, perfringolysin O, theta-toxin, of *Clostridium perfringens*, phallolysin, phallotoxin, streptolysin, and analogs and derivative thereof.

15. (Original) The method of claim 14, wherein the cytolytic peptide is selected from the group consisting of amoebapores, amoebopore analogs and amoebopore derivatives.

16. (Original) The method of claim 14, wherein the procytotoxin has the following structure: Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys(R)-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys(R)-Leu-Ile-Gln-Leu-Ile-Glu-Asp-Lys(R), wherein R is independently selected from the group consisting of the unmodified ϵ -amino group of the adjacent lysine residue, $[\epsilon\text{-}\gamma]\text{-Glu}$, $[\epsilon\text{-}\gamma]\text{-}$

Glu-[α - γ]-Glu₁₋₃, [ϵ - α]-Phe₁₋₃, [ϵ - α]-Tyr₁₋₃, [ϵ - α]-Trp₁₋₃, [ϵ - α]-Lys₁₋₃ and [ϵ - α]-Arg₁₋₃, wherein [ϵ - γ] represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate, [α - γ] represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate, [ϵ - α] represents a peptide bond between the epsilon amino acid of lysine and the alpha carboxyl group of the indicated amino acid and the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

17. (Original) The method of claim 14, wherein the cytolytic peptide is a melittin, a melittin analog or a melittin derivative.

18. (Original) The method of claim 17, wherein the procytotoxin has the following structure: Gly-Ile-Gly-Ala-Val-Leu-Lys(R)-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Lys(R)-Arg-Lys(R)-Arg-Gln-Gln, wherein R is independently selected from the group consisting of the unmodified ϵ -amino group of the adjacent lysine residue, [ϵ - γ]-Glu, [ϵ - γ]-Glu-[α - γ]-Glu₁₋₃, [ϵ - α]-Phe₁₋₃, [ϵ - α]-Tyr₁₋₃, [ϵ - α]-Trp₁₋₃, [ϵ - α]-Lys₁₋₃ and [ϵ - α]-Arg₁₋₃, wherein [ϵ - γ] represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate, [α - γ] represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate, [ϵ - α] represents a peptide bond between the epsilon amino group of lysine and the alpha carboxyl group of the indicated amino acid and the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

19. (Original) The method of claim 17 wherein the procytotoxin has a structure selected from the group consisting of: N-Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys-Ile-Gln-Leu-Ile-Glu-Asp-Lys([ϵ - γ]-Glu-[α - γ]-Glu)-COOH and NH₂-Gly-Ile-Gly-Ala-Val-Leu-Lys-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Lys([ϵ - γ]-Glu-[α - γ]-Glu)-Arg-Lys([ϵ - γ]-Glu-[α - γ]-Glu)-Arg-Gln-Gln-COOH.

20. (Previously Added) The procytotoxin of claim 2, wherein the pore-forming cytolytic peptide is selected from the group consisting of Ae I, cytolysin of sea anemone, aerolysin, amatoxin, amoebapore, amoebapore homolog from *Entamoeba dispar*, brevinin-1E, brevinin-2E, barbatolysin, cytolysin of *Enterococcus faecalis*, delta hemolysin, diphtheria toxin, El Tor cytolysin of *Vibrio cholerae*, equinatoxin, enterotoxin of *Aeromonas hydrophila*, esculentin, granulysin, haemolysin of *Vibrio parahaemolyticus*, intermedilysin of *Streptococcus intermedius*, the lentivirus lytic peptide, leukotoxin of *Actinobacillus actinomycetemcomitans*, magainin, melittin, membrane-associated lymphotoxin, Met-enkephalin, neokytorphin, neokytorphin fragment 1, neokytorphin fragment 2, neokytorphin fragment 3, neokytorphin fragment 4, NK-lysin, paradaxin, perforin, perfringolysin O, theta-toxin, of *Clostridium perfringens*, phallolysin, phallotoxin, and streptolysin.

21. (Previously Added) The procytotoxin of claim 20, wherein the cytolytic peptide is an amoebapore.

22. (Previously Added) The procytotoxin of claim 21, having the following structure: Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys(R)-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys(R)-Leu-Ile-Gln-Leu-Ile-Glu-Asp-Lys(R), wherein R is independently selected from the group consisting of $[\epsilon\text{-}\gamma]\text{-Glu}$, $[\epsilon\text{-}\gamma]\text{-Glu-}[\alpha\text{-}\gamma]\text{-}(Glu)_{1\text{-}3}$, $[\epsilon\text{-}\alpha]\text{-}(Phe)_{1\text{-}3}$, $[\epsilon\text{-}\alpha]\text{-}(Tyr)_{1\text{-}3}$, $[\epsilon\text{-}\alpha]\text{-}(Trp)_{1\text{-}3}$, $[\epsilon\text{-}\alpha]\text{-}(Lys)_{1\text{-}3}$ and $[\epsilon\text{-}\alpha]\text{-}(Arg)_{1\text{-}3}$, wherein:

$[\epsilon\text{-}\gamma]$ represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate,

$[\alpha\text{-}\gamma]$ represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate,

$[\epsilon\text{-}\alpha]$ represents a peptide bond between the epsilon amino acid of lysine and the alpha carboxyl group of the indicated amino acid, and

the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

23. (New) The procytotoxin of claim 22, wherein R is independently selected from the group consisting of $[\epsilon\text{-}\gamma]\text{-Glu}$ and $[\epsilon\text{-}\gamma]\text{-Glu-}[\alpha\text{-}\gamma]\text{-}(Glu)_{1\text{-}3}$, wherein:

$[\epsilon-\gamma]$ represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate,

$[\alpha-\gamma]$ represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate, and

the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.